Time For An Organized Cervical Cancer Screening in Bharatpur, Nepal.

By
Sherpa, Ang Tshering Lama

Supervisor:

Professor Johanne Sundby
Department of International Health
Institute of General practice and Community Medicine
University of Oslo, Norway

Co-supervisors:

Professor Steinar Thoresen
Cancer Registry, Norway

Dr. Mari Nygard
Cancer Registry, Norway

Dr. Balman Singh Karki
B.P.K.M.C.H. Bharatpur, Nepal

Research Collaborators:

Dr.Siliva Franceschii
IARC Lyon, France

Dr.Gary Clifford
IARC Lyon, France

University of Oslo
Faculty of Medicine
Department of General Practice and Community Medicine
Section for International Health
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A. Dedicated to

The man, my brother Tshewang N. Sherpa Lama

For introducing me to the world of science “the medicine.”

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To the woman, his better halve and my sister in-law

For supporting his decision, sacrificing her own needs and desires.

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Where there is love and harmony with no glimpse of gender discrimination.

B. Abbreviations

Alliance for Cervical cancer prevention **(**ACCP**)**

World health organization (WHO)

B.P.Koirala Memorial Cancer Hospital (BPKMCH)

International Agency for Research on Cancer (IARC)

Loop Electro Excision Procedure (LEEP)

European Research Organization on Genital Infection and Neoplasia (EUORGIN)

Squamocolumnar Junction (SCJ).

Transformation zone (TZ)

Human papilloma virus (HPV)

The Bethesda system (TBS)

Carcinoma in Situ (CIS)

Cervical Intraepithelial Neoplasia (CIN)

Squamous intraepithelial lesion (SIL)

Atypical squamous cells (ASC)

Atypical squamous cells of undetermined significance (ASCUS)

Atypical glandular cells of undetermined significance (AGUS)

Low grade squamous intraepithelial lesion (LSIL)

High grade squamous intraepithelial lesion (HSIL)

Federation of gynaecology and obstetrics (FIGO)

Visual inspection with acetic acid (VIA)

Human papilloma virus (HPV)

Human Papilloma virus deoxyribonucleic (HPV DNA)

Visual inspection with Lugol's iodine (VILI)

Papanicolaou smear (Pap smear)

International Union against Cancer (UICC)

Female community Health Volunteer (FCHV)

Community Health Volunteer (CHV)

United nation population fund (UNFPA)

German agency for technical cooperation (GTZ)

Sexually Transmitted infection (STI)

Sexually Transmitted disease (STD)

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D. Abstract

Background

Cervical cancer is the most common cancer in Nepal and most often they are diagnosed as stage 2 or more. Despite having country's cancer referral hospital B.P Koirala Memorial Cancer Hospital (BPKMCH), the biggest well equipped in terms of infrastructure, treatment facility and expert manpower is in Bharatpur, organized cervical cancer screening service is not yet exists in this area.

Objective

To start a new programme like this it is essential to assess a cervical cancer program and its ability to detect a proportion of possible abnormal cervical smear and assess women's barrier for attending cervical cancer screening service. Thus the present study aims at identifying determinants of these factors that are necessary for successful cervical cancer screening programme in Bharatpur, Nepal.

Methods

Population based cross sectional study was carried out from October 2006 to march 2007. 1547 ever married women aged 15-59 were selected with cluster randomization procedure from ward number 11 Bharatpur municipalities. Ethical clearance to carry out this study was sought from Nepal Health Research council (NHRC) ethical clearance committee. Pap smear test was carried out in BPKMCH and reporting was done on Bethesda system. Interviews were performed using a standard questionnaire pertaining to socio-demographic and reproductive characteristics, their awareness and knowledge regarding cervical cancer and their barriers to utilize the cervical cancer screening service.

Results

Out of 1547 total study population 1033 participated in the study and 977of them had Pap smear. Proportion of abnormal cervical smear detected in this study includes ASC: 2.86%, LSIL: 0.2% and HSIL: 0.5%. Thus total prevalence of different grades of abnormal cervical smear was found to be 3.5%. Those who had previous Pap smear 29% belongs to women aged 16-29, 46.6% with aged 30-44 and 42% with aged 45-59.

Though 40% have heard of cervical cancer only 26% have responded correctly about the possible prevention and 24.7% responded correctly for its treatable nature when diagnosed early. Health workers role for information dissemination was found lower (47.8%) than mass media and social networks78.5% & 78.5% respectively.

Increase proportion of women with awareness of cervical cancer is noted as education level increases and chances of having previous Pap smear among women who have heard of cervical cancer is noted twice than those who have not heard. These differences in proportion were significant with P value of 0.000.

33.2% of the total study population were non participant. Among them 71% were from non slum area compared to 29% from slum area. Major determinants of these women's barrier were their lack of perception about preventive role of Pap smear, lack of time and lack of permission from there husband to go to cervical cancer screening.

Conclusion

Proportion of women with HSIL in our study was not more than other study in developed country, yet cervical cancer is number one malignancy in Nepal. Existence of many societal behavioural patterns in Nepal that are risk to cervical cancer and present opportunistic cervical cancer screening services which have low coverage rate of cervical cancer screening for women with aged 30s and 40s who are considered highest risk group makes the establishment of organized screening service a must.

Favourable rate of participation from women with lower socio economic status in our study could be due to free cervical cancer screening service that we have provided. Therefore to reach women with lower socioeconomic status the screening fee must be very nominal. Awareness of cervical cancer is crucial factor to increase cervical cancer screening coverage. Dissemination of proper information to the women, their husband and community at large and inclusion of women's barrier in the community to cervical cancer information is a pre-requisite to have increase cervical cancer screening coverage.

Key words: Cervical cancer, prevalence, abnormal cervical smear, Pap smear, coverage, organized cervical cancer screening, awareness, knowledge, barriers, Bharatpur, Nepal.

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E. Introduction

Global Magnitude of the Cervical Cancer

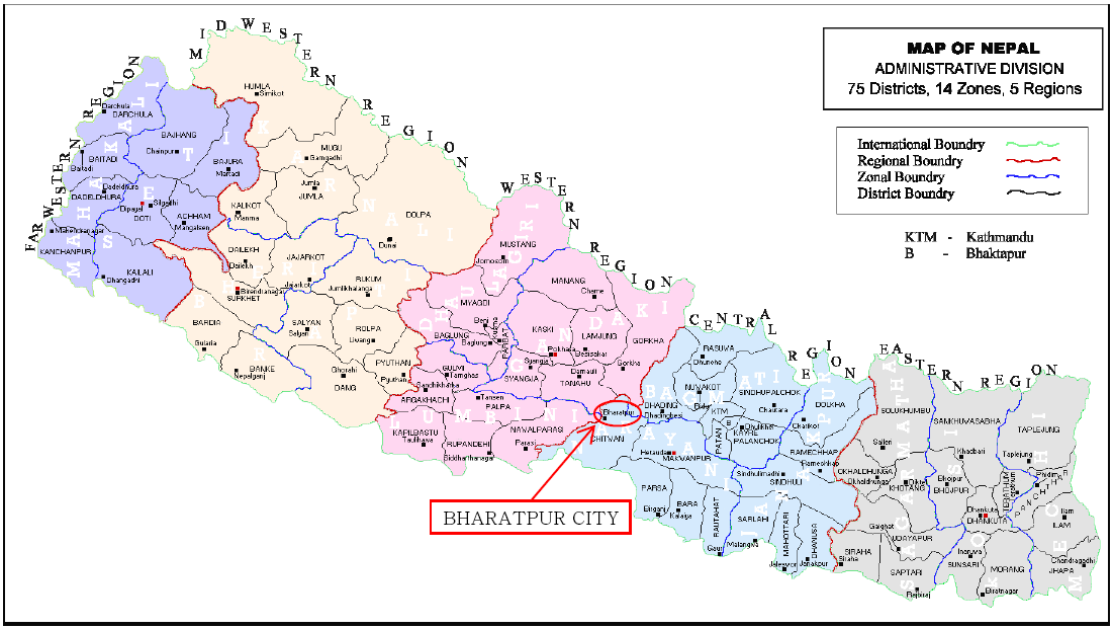
According to Alliance for Cervical Cancer Prevention (ACCP) 2004, cervical cancer is the most common form of cancer in women in virtually all developing countries

and the second most common form of cancer in women in the world following breast cancer. (1) It constitutes approximately 12% of all cancers in women. Globally, 500,000 new cases are diagnosed every year and 300,000 deaths are secondary to cervical cancer. Among these global estimates 80% harbors in developing countries. (2)

Early detection and screening along with health education programmes have been successful in reducing morbidity and mortality up to 80%, in most developed countries.(2)

Background of the Country

Nepal is landlocked country bordering China in the north and India on south. Topographically it is divided into three distinct ecological zones (mountains, hills and Terai).Total area of the country is 147,181 square kilometers. Terai (plain) covers 34,019 square kilometer and is inhabited by 49 percent of the population.



Map of Nepal

Basic Demography and Health Indicators of Nepal

Indicator	Value/Nominator
Total population (2001)	23.5 million
Annual population growth rate	2.27
Life expectancy at birth	59.7
Total fertility rate (2001)	4.1
Contraceptive prevalence rate (2001)	39.3
Maternal mortality ratio (1999)	539/100 000
Age at first marriage (women)	16.7 years
Adult female literacy rate (2001)	28.7%

Risk factors for Cervical Cancer

It has been already documented that acquisition and interaction with certain subtypes of Human papilloma virus (HPV) such as type 16,18, 31 ,33 etc which are considered as high risk HPV(hr-HPV) is the central necessary cause for cervical cancer.[3] Cofactors such as high parity, oral contraceptive use, smoking etc are also risk factor for acquiring cervical cancer.[2]Thus in our setting socio-demographic indicator of the country itself is a risk factor for acquiring cervical cancer with early childbirth in consequence of early marriage, low women literacy rate, high fertility rate and majority of the population with poor socioeconomic status. [4]

Magnitude of the cervical cancer in Nepal:

According to World health organization (WHO), 2002 China and India had 131,500 and 125,952 new cases of cervical cancer per year respectively. [5]Based on these two neighbor countries incidence data and based on similar socio-cultural pattern between Nepal and India, we can predict that Nepal must have alarming incidence rate for cervical cancer. This is further supported by finding in the hospital based cancer registry in B.P.Koirala Memorial Cancer Hospital (BPKMCH). Cervical cancer is the most frequently detected malignancy in Nepal.[6] Population based cancer registry is not available in Nepal and also prevalence and incidence of cancer at population level is not yet known. A population based study including 5000 women aged 30-59, carried out in 2003 in collaboration between BPKMCH and

International Agency for Research on Cancer (IARC) found 2.5% prevalence for precancerous lesion and 0.12 % for invasive cancer.

Health Facility Pertaining to Cervical Cancer at Study Area

BPKMCH, the biggest cancer referral hospital (100 beds, established in 1996) is located in Bharatpur, Chitawan, in Terai region, 150 km south west from the capital (Kathmandu). The hospital consist of all units relevant to cervical cancer including gynecology oncology unit, radiation oncology unit, anesthesia, pathology, radio diagnosis and imaging and cancer prevention, control and research and palliative therapy.

Examinations to Papanicolaou smear (Pap smear), Colposcopy, Cervical Biopsy, Endometrial Biopsy, Endocervical Curettage, Cryotherapy and Loop Electro Excision Procedure (LEEP) were routinely performed in gynecology unit and the services are provided by gynecologist. Radiation oncology unit consist of radiation oncologist, physicist, technologist and technicians and among other services they also offer brachytherapy. Pathology department routinely provide other required service for cancer patient including cytopathology and histopathology. The pathology department consists of 4 pathologist, 4 technologists, 1 senior technician and 8 technicians.

Despite having human resources, technical facility for diagnosis and treatment and expert manpower the hospital has no organized screening system for the most commonly occurring cancer (cervical cancer). Opportunistic cervical cancer screening is provided once a week. Cancer awareness and education program is run in out patient department daily to increase awareness among patients, visitors and attendants. FM radio stations, cervical cancer pamphlets and Pap smear leaflets written in Nepali language were also used for public awareness.

Due to the availability infrastructure for diagnosis and treatment and human resources, particularly speaking of Bharatpur, Chitawan where BPKMCH is located it is foreseeable to establish an organized Cervical Cancer screening in that area.

Rationale to carry out this study

However cervical cancer is most frequently occurring malignancy in Nepal, most of the studies carried out in Nepal in regards to cervical cancer are hospital based [7, 8] and despite extensive literature search, research that assess target women's awareness and knowledge regarding cervical cancer or identifying the determinants of non participation of the target

women in cervical cancer screening services were not found. Thus the present study aims at identifying determinants of these factors that are necessary for successful cervical cancer screening programme in Bharatpur, Nepal.

Chapter 1 : Review of literature

1.1 Magnitude of Cervical Cancer Globally

Central and south America, the Caribbean, Sub-Saharan Africa part of Oceana, south and south east Asia are the regions with highest incidence rates of cervical cancer-over 30 per 100,000 women.[9] This shows that Cervical Cancer is an important public health problem among these developing countries. Global cancer report, 2003 has stated that the global cancer rate could increase 50% by the year 2020.[10] This statement is further highlighted by Peter Boyle the director of International Agency for Research on Cancer (IARC) in European Research Organization on Genital Infection and Neoplasia (EUORGIN) 2004 conference by saying "If nothing is done to prevent cervical cancer, there will be one million women developing the disease annually by 2050 and also the poorest part of the world will be worst affected".[11]

At present approximately 1.5 million people women worldwide are living with cervical cancer, and based on the natural history of cervical cancer up to 7 million women worldwide, may have precancerous condition that need to be identified and treated.[9]

1.2 Patho-physiology of the Cervix

Cancer of the cervix uteri is the cancer that occurred in the lower one third of uterus and is composed of dense fibro muscular tissue lined by two types of epithelium: Squamous epithelium and columnar epithelium. Squamous epithelium covers the most of ectocervix and vagina. Columnar epithelium lines the cervical canal and extends outward to variable portion of ectocervix.The demarcation line between squamous and columnar lining of epithelium is termed as squamocolumnar junction (SCJ). The location of the original SCJ varies with the woman's age, hormonal status, history of birth trauma, pregnancy status and use of oral contraceptives.

When exposed to the acidic environment of the vagina, the normal replacement process termed, squamous metaplasia takes place and gives rise to new SCJ. The area between the new SCJ and original SCJ is termed as transformation zone (TZ). The most abnormal area of the cervical TZ are considered as site where potential preinvasive lesion may reside.[12] In the presence of persistent Human papilloma virus (HPV) infection or presence of other cofactors, the metaplastic squamous cells of TZ take an abnormal appearance, which is called cervical

squamous precancer (dysplasia). These cells later multiply in a disorderly manner typical of cancerous change to produce squamous cell cancer.

Cervical cancer is a progressive disease with histologically detectable pre-invasive stages. Mild, moderate, severe dysplasia and carcinoma in situ are four classical categories of non invasive neoplasia. The morphological criteria used to differentiate these categories are based on degree of epithelial differentiation. Degree of epithelial differentiation becomes progressively obvious along a scale from mild dysplasia to carcinoma in situ.

1.3 Terminologies on Epithelial Differentiation

There were different terminology developed in different period of time to define the neopastic changes and synonymous terminologies are shown below:

Dysplasia	Original CIN	Modified CIN	The Bethesda system (TBS)
Normal	Normal	Normal	Within normal limits, Benign cellular changes (Infection or repair)
Atypia	Koilocytic atypia Flat condyloma	Low grade CIN	LSIL
Mild dysplasia	CIN1	Low-grade CIN	LSIL
Moderate dysplasia	CIN2	High-grade CIN	HSIL
Severe dysplasia	CIN3	High-grade CIN	HSIL
Carcinoma in situ	CIN3	High-grade CIN	HSIL
Invasive carcinoma	Invasive carcinoma	Invasive carcinoma	Invasive carcinoma

CIN: Cervical Intraepithelial neoplasia; LSIL: Low-grade squamous intraepithelial lesion; HSIL: High-grade squamous intraepithelial lesion; ASCUS: Atypical squamous cells of undetermined significance; AGUS: Atypical glandular cells of undetermined significance.

Carcinoma in Situ (CIS) was introduced in 1932 to denote those lesions in which the undifferentiated carcinomatous cells involved the full thickness of the epithelium, without disruption of basement membrane. The term dysplasia was introduced in the late 1950 to designate the cervical epithelial atypia that is intermediate between the normal epithelium and CIS. Dysplasia was further categorized into three different groups-mild, moderate and severe depending upon the degree of involvement of epithelial thickness by the atypical cells

Cervical intraepithelial Neoplasia (CIN) was introduced in 1968 to denote the whole range of cellular atypia confined to the epithelium. Increase recognition of pathological changes such as koilocytic or condylomatous atypia with HPVinfection around 1980 led to development of modified CIN terminology in 1990 and which showed that high grade CIN are considered to be true precursor of invasive cervical cancer.

In 1988 the US National Cancer institute convened a workshop to propose a new scheme of classification for reporting cervical cytology reports and developed the new term the Bethesda system(TBS) in1991.This system is also recommended by WHO to report Pap smear.[13]

1.4 The Bethesda System of Reporting Pap Smear

The main feature of TBS was the creation of term squamous intraepithelial lesion (SIL) and two grade scheme consisting of low grade (LSIL) and high grade (HSIL) lesions. TBS combines flat condylomatous (HPV) changes and low grade CIN (CIN1) into LSIL, While the HSIL encompasses CIN2 and CIN3.The term lesion was used to emphasize that any of the morphological changes upon which a diagnosis is based do not necessarily identify neoplastic process. TBS was reevaluated and revised in 2001 workshop convened by the National Cancer Institute, USA, cosponsored by 44 professional societies representing more than 20 countries. The reporting categories under the 2001 TBS includes Negative for intraepithelial lesion or malignancy, Squamous cell abnormalities, Glandular cell abnormalities and Endometrial cells in a woman over 40 years of age.[14]

1.5 Natural History of Dysplasia

It now appears that the direct precursor of cervical cancer is high grade dysplasia, which is about a third of instance may progress to cervical cancer over a period of 10 to 15 years, while most low grade dysplasia regress spontaneously.[15,16]

A Meta- analysis of 27,000 women gave the weighted average rates of progression to HSIL and invasive cancer at 24 months according to baseline cytological abnormality of ASCUS, LSIL and HSIL. This showed that 68.2% of ASCUS, 47.4% of LSIL and 35.0%of HSIL regress to normal at 24 months and 7.1% of ASCUS, 20.8% of LSIL progress to HSIL and 23.4% of HSIL remain persistent. The study also showed that 0.3% of ASCUS, 0.2% of LSIL and 1.4% of HSIL progress to cervical cancer at 24 months. [17]

1.6 Stages of Cervical Cancer

According to Federation of gynecology and obstetrics (FIGO) classification, Cervical Cancer is classified into stage 1 to 4. [18] The Staging was done based on the presence of cancer that is confined to the cervix (stage 1), invading beyond the cervix but not to pelvic wall or lower third of vagina (stage 2), extending to pelvic wall or lower third of vagina or causes hydronephrosis (stage 3) and extending the bladder or rectal epithelium or beyond the true pelvis (stage 4). Treatment ranges from cone biopsy, Loop electrosurgical excision procedure (LEEP) or hysterectomy to pre invasive stages and hysterectomy or radiation therapy or combination of both depending upon the stage of the disease.5 year survival with optimal treatment ranges from 90 to 100% in stage 1A to 0% in stage 4B. Thus the cure rate for invasive cervical cancer is closely related to the stage of disease at diagnosis and the availability of treatment. [19]

A study in Iceland has shown that a cervical cancer screening programme helps to reduce incidence of stage 2 and more advances stage of cervical cancer. [20]

A study conducted in Nepal, by Zhang et al. showed that 90% of the invasive cancer is squamous cell carcinoma and most often detected at a very late stage, stage >2. [21] This could be attributed to lack of an organized screening system, poor health facilities and the poor socioeconomic status of women in Nepal.

1.7 Risk Factors for Cervical Cancer

The majority of cervical cancer cases are caused by hr-HPV, a sexually transmitted virus that infect cells and may result precancerous lesion and invasive cancer. [3,23] Though exposure of HPV infection to sexually active women are very common, most cervical abnormalities caused by HPV regress themselves and only few progress to high grade CIN or cervical cancer. The long duration that takes for manifestation of overt disease from the initial infection of HPV showed that other cofactors influence the progression of disease. The cofactors include HPV related cofactors: viral type, simultaneous infection with several oncogenic types, high virus load, host related cofactors: immune status and parity and exogenous cofactors: Tobacco smoking, coinfection with HIV or other sexually transmitted agents such as Herpes simplex virus 2(HSV-2), *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and long term (>5years) use of oral contraceptives. [24]

1.8 Preventive Approach to Control Cervical Cancer

Primary prevention, early detection through increased awareness and organized screening programme, diagnosis and treatment are four components of cervical cancer control.

Progression from cervical lesions to invasive cancer is a slow process and most often it is asymptomatic in its early stages. Therefore an early detection and treatment of these asymptomatic lesions can only be possible if women are given opportunity to have cervical cancer screening at an early stage.

1.8.1 Cervical Cancer Screening

According to WHO, screening is a public health intervention used on a population at risk, or target population to identify individuals with high probability of having or developing a disease but not undertaken to diagnose a disease. Thus screening is the process by which a test is applied to select out asymptomatic individuals at risk of having or developing a certain disease.

Several tests such as Visual inspection with acetic acid (VIA), Visual inspection with Lugol's iodine (VILI), Human Papilloma virus deoxyribonucleic (HPV DNA) test and Pap smear test can be used in screening for cervical cancer. But to date, the Pap smear is the only test that has been used in large population for more than 50 years and it has shown tremendous effect in reducing incidence and mortality from cervical cancer. According to IARC estimate, among well-screened women aged 30-64 years, Pap smear screening prevented 80% of cervical cancers. [23] Present HPV DNA test may not be feasible in low resource country due to high cost and lack of technical facility and VIA or VILI which has been advocated as alternative strategies for screening cervical neoplasia in low resources country has still not developed comparable evidence on their effectiveness and large studies are still underway.[25]

Though specificity of Pap smear is generally agreed over 90% its limited sensitivity has been acknowledged openly and it has been estimated to be range from 50-80%.[26] But this lower sensitivity is masked by regular screening, which has cumulative sensitivity of over 90% for three successive smear. [27]

A study conducted in Nordic countries has showed 93% sensitivity of Pap smear test in the 25-64 year age group at an interval of one year and 73% after 3 years and specificity of approximately 98%. Same study also concluded that the sensitivity at 3 years was 91% for squamous cell carcinoma and 58% for adeno and adenosquamous carcinoma. [20] A hospital based study conducted in one of the laboratories in teaching hospital in Kathmandu also

showed significant correlation of Pap smear result with result of histology. The study has shown76% sensitivity and 83.3% specificity for diagnosis of benign grade, 60% sensitivity and 93.9% specificity for LSIL, 100% sensitivity and 89.5% specificity for HSIL and 100% sensitivity and specificity for carcinoma. [28]

Past failure in cervical cancer screening in developing countries are primarily due to quality of screening programme than technological limitation of screening test.[29] This infers that shift in paradigmatic focus from technology toward quality is mandatory and more fundamental and challenging issue is the organization of the program in its totality. Report of WHO consultation also says that the essential element for successful cytology include training of the relevant health care professionals, including smear takers, smear reader (cytotechnologist and cytopathologist), colposcopist and program managers.[25]

Screening programme is defined as opportunistic when the initiative to screening is done by the person or health care provider without regard of previous screening. Whereas, an organized screening is the programme that invites all persons at regular intervals regardless of opportunistic screening. According to WHO for a screening programme to be successful, following elements must be present :[13]

♦high coverage (80%) of the population at risk of the disease.

♦Appropriate follow up and management for those who are positive on screening.

♦Effective links between programme components (e.g. from screening to diagnosis and treatment)

♦high quality of coverage, screening tests, diagnosis, treatment and follow up.

♦Adequate resources.

According to International Union against Cancer (UICC) organized screening is more effective than opportunistic screening in reducing the risk of cancer, because of its ability to achieve higher compliance by the risk groups and is also more cost effective as it prevents over use of services. [30]

1.8.2 Effect of Cervical Cancer Screening in Developed Countries

Organized screening programme was started as early as 1949 in British Columbia in Canada. By1960 there were screening programme in much of Scandinavia. A sharp decline in the incidence rate and mortality rate of cervical cancer was observed in many developed countries within the last 40 years due to organized screening program. The Nordic countries are exemplary in this respect. Nordic countries (Iceland, Finland, Sweden, Denmark) which have

initiated organized screening program much earlier around 1960 showed higher rate of reduction in incidence and mortality of cervical cancer, compared to Norway where organized screening was initiated much later around 1994. [31, 32] Study conducted in Norway has also shown that increase coverage of target population has significant role in reducing invasive cervical cancer. [33]

1.8.3 Failure of Cervical Cancer Screening in Developing Countries:

Despite tremendous positive impact of cervical screening in developed countries, most middle income developing countries where the screening program has initiated as early as 1970 such as Cuba, Mexico, Colombia etc, have seen no but no substantial decrease in mortality from cervical cancer. This is attributed to unrealistic notion of frequent cervical cancer screening offer to targeted women of wide range of years (20-65). [34] A study pertaining to African country also showed that the existing programs are failing to achieve a major impact due to relying on opportunistic screening of relatively young women; lesser target for women in risk groups (women in their thirties and fourtees) and low levels of coverage with at least once in a lifetime screening for at-risk women. [35]

Thus looking back to screening program in most developing and developed countries one can conclude that to obtain positive impact on cervical cancer incidence and mortality, efforts must be focused on improving screening coverage rates for high risk targeted women. However, obtaining high level of coverage is challenging in both developed and developing countries.

In developing countries the barriers to cervical cancer screening uptake include absence of knowledge about the disease, lack of familiarity with the concept of preventive health care, geographic and economic inaccessibility of services, poor quality of services and lack of support from families and communities. [36] Several studies have shown that a lack of awareness about cervical cancer and how to prevent it is an important obstacle to improve screening coverage. [37, 38, 39, 40]

A big case control study conducted in Maharashtra, western India including 97000 women in cases and 79,000 women in control group showed that efforts to improve awareness of the population has resulted in early detection of and improved survival from cervical cancer.[34]

Chapter 2 :Objectives of the study

2.1 General Objectives:

2.1.1 To study a cervical cancer program and its ability to detect a proportion of possible abnormal smear in a female population in Nepal.

2.1.2 To assess women's barrier for attending cervical cancer screening in Nepal.

2.2 Specific Objectives:

2.2.1 To estimate the prevalence of abnormal Pap smears finding among women in Bharatpur.

2.2.2 To assess women with at least one previous Pap smear among married women aged 30-59 in Bharatpur.

2.2.3 To assess women's awareness about cervical cancer among married women in Bharatpur.

2.2.4 To assess knowledge about cervical cancer among married women aged 30-59 in Bharatpur.

2.2.5 To identify the barriers that hinders women to participate in a cervical cancer screening clinic.

Chapter 3: Methodology

3.1 Study Design:

A community based cross sectional study was carried out among 1547 married women aged 15-59 living in Bharatpur municipality of Chitawan district in Nepal.

Structured interview questionnaire were used for data collection. However, in-depth information regarding awareness and knowledge of cervical cancer, barriers to utilization of preventive health services and information regarding sensitive issues such as multiple sexual partner can be identified in more detail through either using open ended questionnaire or qualitative study such as focus group discussion, participatory observation etc but due to limitation of time the study was not carried out in such a way and we acknowledged for that.

3.2 Study Area:

Chitawan district consist of 13 county with, 36 village development committee and 2 municipality with total population of 4,69,699.The total area is 2238.39 square kilometer and among them 40.60% of land is occupied by national park,4.58% by urban and 54.82% by rural area.

This district lies in the center of the main East -West highway of the country, 310 meters above the sea level and is approximately 150 km south west from Kathmandu, the capital and takes about 10 minutes by air and four hours by road.

Bharatpur municipality occupies 68.77 square kilometer of the total land of Chitawan.

It consist of fourteen wards with total population of 54,670 and among them 26289(48%) are female with mixed population of urban and rural area. [(4)]

The prime reason that Bharatpur municipality, Chitawan is chosen for this study is because of BPKMCH is situated here. Thus even after the completion of the study those participant who will be diagnosed to have abnormal smear such as ASCUS, LSIL and HSIL who need further diagnosis and management can be referred to this hospital and treatment will be provided to those who need according to hospital protocol.

For our study, ward number 11 of Bharatpur municipality was chosen. This ward consists of 2326 households with total population of 10,740 (5475 male and 5265 female). Uniqueness of this ward is that it consists of household from slum area and from non slum area and also inhabited by marginalized ethnic groups such as Darai and Kumal. [(4)] Thus we tried to get good representation of total population.

A household from Slum area

3.3 Study Populations:

3.3.1 Sample size for the Proposed Study:

Based on population based study carried out between BPKMCH and IARC in 2003, [5] the prevalence of precancerous lesion for cervical cancer was found to be 2.5%. Sample size of our study was calculated based on this previous prevalence in this area.

The minimum number of participants required for this study was calculated using the formula **$N= R/E^2$**; Where N = minimum number required, R= rate of prevalence, E= Standard error

Standard error was calculated to be 0.5/100, considering the expected prevalence range from 1.5 to 3.5%.

Rate= 2.5/100= 0.025

Error= 0.5/100= 0.005

N= 0.025/ $(0.005)^2$ = **1000 participants.**

1000 is the required sample size to estimate the prevalence of 1.5 to 3% of abnormal cervical smear detection on cervical cancer screening. But considering possible decrease response rate or refusal to undergo gynecological examination we increased our sample size by 55%. Thus we took total of 1547 married women in our study.

3.3.2 Sample Population

Married women aged 15.-59 residing in Ganeshthan, Muktinagar, Naurange and Bhojad from ward number 11, Bharatpur municipality were chosen.

1000 is the required sample size to estimate the prevalence of 1.5 to 3% of abnormal cervical smear detection on cervical cancer screening. But considering possible decrease response rate or refusal to undergo gynecological examination we increased our sample size by 55%. Thus we took total of 1547 married women in our study.

3.3.3 Sampling Process

Though it is ideal to do the individual random sampling process we found its difficult to randomize individual when considering the providing service like cervical cancer screening. Thus instead we did cluster randomization and thus selected Ganeshthan, Bhojad, Muktinagar, Naurange and Lama Tole from ward number 11.

3.4 Inclusion Criteria

Married women aged 15-59 from Ganeshthan, Muktinagar, Naurange and Bhojad of ward number 11, Bharatpur municipality.

3.5 Exclusion Criteria

- ♦ had undergone hysterectomy for any cause.
- ♦ had undergone cervical cancer treatment or those who are under treatment of cervical cancer
- ♦ those that was severely ill to come to the screening clinic.
- ♦ those that was pregnant at the time of our study.
- ♦ those who did not gave consent to participate in the study.
- ♦ those who are heavily menstruating (called for later date, after 2 weeks)

3.6 Research Team at Field Work

Research team at the field consists of following persons:

- ♦ Two female interviewers with collage degree.
- ♦ Two Female Community Health Volunteers (FCHV) that are also lives in our study site.

♦ A smear taker nurse with 20 years experience working in family planning and with very good experience in speculum examination and smear collection.

♦ An assistant nurse.

♦ A medical doctor with two years training in obstetrics and gynecology department,

♦ Myself, the principal investigator with eight years experience working in various medical field after graduation.

♦ An experienced medical technologist who deals entire Pap staining in BPKMCH.

♦ An experienced pathologist from BPKMCH who had also done her doctorate thesis in Pap smear.

♦ A gynecologist from BPKMCH to deal women with abnormal smear for further management and treatment.

♦ Director of BPKMCH to supervise the project work.

♦ Two data entry personnel with good technical skills in computer.

3.7 Training for Field Workers

Training was basically given to interviewers, FCHV and data entry personnel and nurse. All of them were given two lecture class about what cervical cancer is, its causes and risk factor and measures to prevent cervical cancer, the interviewer were further explained about each question and taught how to conduct interviews and how to report exactly how the respondent will answer, to keep the confidentiality of the information that they will gather during field work and to remain non judgmental for participants response. FCHV were familiarized about the house mapping done by the interviewer how to record the invitation card and logbook. Data entry personnel were also explained about how to record exactly as it is in the questionnaire in the excel data base.

Several meetings were also held between research team for discussion of problems, maintaining good morale. From the very early part of study, before starting the actual field work our collaborator from IARC Dr. Silvia Franceschi came to Nepal and guided us how to run this project and at the start of project Dr. Gary Clifford spent one week for actual data collection in the field and data management.

3.8. House Mapping

Given the fact that the demographic distribution of the population is not well known initial survey was done every household in ward number 11 and questionnaire were asked how

many married women aged 15-59 lives in each household and at the same time numbering of the house were also done by the permanent marker pen. The house mapping were done by the two personnel who were interviewer in our research team and after completion of the house mapping community health volunteers who will be recruiting these women were also familiarized about the house mapping. The reason that two interviewer were employed in house mapping instead of FCHV who actually recruit that participant was because the interviewer are more efficient in doing this task since they are younger, energetic and also know how to ride bicycle. During this time women in these household were also asked about their willingness to participate cervical cancer screening and very good response was achieved.

Interviewer informing about the objective of the study at the time of house mapping.

Interviewer writing household number with permanent marker pen.

3.9 Pilot Study

Pilot study was conducted for 10 women. At this time we assessed how many will actually undergo gynecological examination, assessed expected time to examine each patient including signing of consent form, interview and gynecological examination. Thus number of participant that can be called in a day was determined. Data collection forms were also assessed to see if it can be filled without any confusion. Questionnaires were assessed if it can be easily understood by participant and reliability of answer was checked by asking same questionnaire by two interviewers to the same informant and comparing the result. After the pilot study following changes were made:

1. Initial thought of inviting 10 women per day was changed to inviting 20-30 women per day.
2. Questionnaire that includes husbands occupation with army was removed since all women at that time did not want to disclose if their husbands are working in the army. From this we derived that this question was not appropriate at that situation since there was internal conflict going on in our whole country and holding position in either form of army were target for each other.

3. Initially when we invite participants we gave them clinic address and told to come on their own and we will be reimbursing the transportation cost but when we did this some of the participants did not come and some participants came very late when the clinic is already closed. So we decided to accompany the invited women by a CHV and bring them to the clinic in a group at one time, preferably between 10-12AM.

4. For Pap smear report distribution we thought of distributing by CHV but many women were found not to receive their report on time or some ever. Thus we decided to call the women by themselves to the screening clinic after 4 to 6 week for follow up of their result.

3.10 Data Collection

3.10.1 Recruitment of the participants

Two FCHV who also lives in ward number 11 were assigned to invite all eligible women in these areas, through door to door personal visit 1 day before the appointment for screening. Each day each CHV visited 10-20 household and distributed the invitation card to those eligible women who were willing to participate. Those women who accept to get the invitation card were assigned a subject identification number.This number is composed of study identifier number (142) followed by the individuals code (4 digits).This information was transferred to invitation card and invitation register including household number, address, full name and age.Next morning each CHV went to these women to bring them to the clinic altogether. Those who got the invitation card but did not participate in the study were recorded as non participant and reason for non participation in the study were asked.

Upon arrival at the study clinic, women will be checked with the Invitation Register, after which information will be given to groups of up to 10-20 women on the study objectives and the benefits of screening. All participants will be asked to sign an informed consent form before the clinical examination and interview. If a woman accepts to either give undergo gynaecological examination, or just respond questionnaire were included in the study.

Principal investigator explaining study objectives to the participant before signing informed consent form.

Field research team with the mothers group “Ama Samuha” and teachers from the study area.

3.10.2 Face to Face Interview

The questionnaire were adapted from previous study questionnaire used for Women's health survey in Norway and questionnaire used for assessment of reproductive morbidity in Nepal conducted by united nation population fund, German agency for technical cooperation and ministry of health, Nepal.[41]

Question prepared in English were converted into Nepali language and these sets of questions converted into English and Nepali were further checked by 3 Nepalese doctors and concluded exact translation.

After an informed consent has been signed an interview about socio-demographic, reproductive health characteristics of participant and their awareness, knowledge and barriers to seek preventive health service for cervical cancer were administered to all participants by female interviewers.

Each woman was interviewed in a confidential manner in complete privacy in a separate room.

At the end of day all questionnaire were checked to see the completeness by finding missing answer.

Tallying similarity of subject identification number in all the forms used and checking completeness of questionnaire.

3.10.3 Pap Smear

3.10.3.1 Cervical Smear Collection:

Either senior nurse or medical doctor was assigned for collecting smear. After the application of speculum smear was collected according to standard protocol using an extended tip plastic Ayre spatula and inserting it to the os and rotating it through the full circle(360 degrees).[12]

Both sides of spatula were smeared onto the frosted glass slide with one or two careful swipes. Labeling of the slide was done by diamond marker pen using same subject identification number which was used in invitation card and questionnaire. Fixation of slides was done immediately by immersing the slide in 95% ethanol for 20-30 minutes and then air dried. All this procedure was carried out taking into consideration of aseptic precaution.

Women with history of discharge with abnormal finding on gynecological examination were referred by the nurse to the medical doctor and given one course of antibiotics according to WHO guidelines. [13]

Details concerning the visual status of cervix and all clinical diagnostic work up procedures were recorded in the clinical examination section of the questionnaire.

Performing speculum examination and collecting cervical specimen with extended tip Ayer's spatula and endocerical brush.
(Picture taken with the permission from the participant)

Wart (cauliflower like overgrowth) around the vulva and discharge per vagina:
Possible HPV infection.
(Picture taken with the permission from the participant)

3.10.3.2 Laboratory test:

After fixing the slides at the screening clinic, they were sent to the pathology laboratory for Pap staining and reporting. Slides were sent in batches about 150 slides every week. All the reading of slides was done by single qualified pathologist, according to the Bethesda system.

3.11 Quality Control of the Laboratory Test:

However quality assurance is crucial in cytology reporting, we would like to acknowledge that we failed to do quality control of the reporting of slides in this study and the reason are as follows:

1. BPKMCH is the biggest cancer referral center in Nepal and there is no reference laboratory available in the country.
2. Even review of slides by the other pathologist during this could not be done due to some pathologist who went to study leave and other available pathologist in the department are busy to cope with regular flow of the patient in the hospital.

Though quality control of the Pap smear reporting was not done but high sensitivity and specificity of the result can be assured by the background of the Pathologist who had done

also doctorate thesis on Pap smear and due to her work experience in Cancer hospital where cervical cancer patient are referred highest in number, however exact data is not available.

High quality staining of Pap smear can be assured by selecting a qualified technologist who also does all Pap staining in the hospital. Adequate collection of cellular material from transformation zone are maintained by using extended tip Ayre spatula supplied by IARC France and Cancer Registry, Norway. The adequacy of smear collection could also be verified by very low percentage (0.8% of the total smear taken) of repeat smear advised by the pathologist due to unsatisfactory smear and most of these occurred among postmenopausal women and in these case due to physiological changes the transformation zone moves in to the endo-cervical canal and which makes difficulty taking proper smear.

3.12 Data Management

A completeness of questionnaire were checked by missing answer and proper matching of subject identification number in all forms used and specimen collected were checked at the end of the day after data collection. Double-entry of the data from questionnaires was performed on a regular basis, almost everyday at the end of data collection by two data entry personnel on Excel (registr.Xls). When Pap smear results were available they were also recorded to database. A copy of the result was provided to the participant themselves and a copy of the result was kept in BPKMCH pathology department for future reference.

3.13 Data Analysis

Data checking were done by comparing the data files entered by two different personnel to reveal if there is any difference between the two files by mistyping. Most of the variables that we have used on our study were categorical data. Thus there were a fixed number of pre-specified values and question that does not apply are coded as 88 and question that was not answered are coded as 99. All erroneous values aside from these specified values are checked and correction was done.

Data recorded on Excel (registr.Xls) was transformed into Statistical program for social sciences (SPSS) program. Data screening were done by producing a histogram and scatter plot of most of the variable to see its normality, average value, outliers and missing values.

Descriptive statistics for categorical variable are obtained by frequencies analysis and mean, median and standard deviation from continuous data are obtained by descriptive analysis. To explore the relationship between different variable and to assess the proportion into different

groups Chi-square test was performed. All analysis was performed using SPSS for Windows (version 12). [42]

3.14 Ethical Consideration

Since this study is part of the bigger study conducted to identify the prevalence of HPV in Bharatpur, in which I myself was the principal investigator, ethical clearance was sought from Nepal Health Research council ethical review board to carry out the Human Papilloma virus study in Bharatpur and to take out the specimen out of the country to perform molecular test. However it was also clearly mentioned that while taking sample for Human Papilloma virus these women will also offered Pap smear test to find out abnormal smear from these women and information will be collected from them regarding risk factor for cervical cancer, cervical cancer awareness and knowledge and barriers for participating in the screening clinic by using some questionnaire.

3.14.1 Scientific Merit

As many studies has proven that cervical cancer screening is cost effective than treating invasive cancer and also organized screening program is more cost effective compared to opportunistic screening service.[12] Therefore this study will help health ministry and governing body to formulate a policy to invest on preventive health, specially in cervical cancer which has multi dimensional, socio-psychological and economic impact not only on woman's life but for the whole family.

3.14.2 Informed Consent

Participants name and address record were recorded on registration log book so that when the results were available they could be easily traced out to handover the result. Beside this participants name and address did not reflect in any other form used, instead each participant was given a identity number to mask the true identity. The same identity number was used on invitation card, questionnaire, and consent form and on Pap smear slides and other specimen collected and Pap smear result. Participants were ensured that the research team guarantees the anonymity of the survey and the confidentiality of the information provided by them.

Participants were given standard information of the purpose and procedure of the study. They were also told that their participation in this study is their own free will and that they were

free to respond either only questionnaire or only undergo gynecological examination or refuse both without jeopardizing their treatment at the clinic.

Participants were also provided antibiotics for free for suspicious genital infection detected at the time of screening. All participants who had Pap smear were given their result and women with abnormal smear (ASCUS and LSIL) are advised for repeat cervical smear after 6 months and HSIL were advised for immediate biopsy. They were also told that these repeat cervical smears, biopsy will be free of cost and treatment will be provided in BPKMCH according to hospital protocol, for those who need.

3.15 Time Allocated for Field Study

House to house survey: 2 week

Meeting with research team to discuss about the project: 1 week

Training for interviewer and assistant: 1 week

Change questionnaire written in English into Nepali language: 1 week

Pilot study: 2 week

Data collection: 3 month (12 weeks)

Miscellaneous activities: 1 month (4 weeks)

Total duration spent for data collection: 23 weeks= 6 months

Chapter 4 Result: Text, Tables and graphs

Table 1. Socio-Demographic Characteristics of Study Population

Total number of participants	1033(70%)
Participants with Hindu religion Participants with Buddhist religion Participants with Christian religion Participants with Moslem religion	871(84.3%) 135(13.1%) 24(2.3%) 3(0.3%)
Mean age of the participants (standard deviation) Minimum-Maximum age of the participant	34.3(10.416) 16-59
Marital status: Married Separated or divorced Widow Remarried	 931(90.1%) 26(2.5%) 31(3.0%) 45(4.4%)
Participant's household From Slum area: Participants household from non slum area	540(52.3%) 493(47.7%)
Participants with history of smoking: Participants who are Past smoker	127(12.3%) 78(7.6%)
Participants occupation: unemployed Housewife Labour worker Vegetable seller/shopkeeper Clerical work Higher level job	 55(5.3%) 773(74.8%) 105(10.2%) 61(5.9%) 36(3.5%) 3(0.3%)
Education: Illiterate Primary Secondary Completed high school Higher degree	 463(44.8%) 184(17.8%) 231(22.4%) 76(7.4%) 79 (7.6%)

Table 1 shows that 1033 women with mean age of 34.3 with minimum age of16 to maximum of 59 have participated in this study and 84.3% of them are Hindu, 44.8% are illiterate, 74.8% are housewife, 2.5% &4.4% divorce or separation rate and remarries rate respectively, 52.3%

are from slum area and 47.7% are from non slum area and 12.3% of women are current smoker.

Table 2. Characteristics of Participant's Husband in Study Population

Table 2.1 Husbands Occupation

Occupation	Number (n)	percentage
Unemployed	94	9.1
Farmer	59	5.7
Labour worker	280	27.1
Shopkeeper	86	8.3
Clerical work	127	12.3
Higher level job	35	3.4
Migrant worker	223	21.6
Driver	29	2.8
Total	1033	100

Table 2.1 Highest proportion (27.1%) of the participants husband were found to be labour worker, followed by 21.6% are migrant worker,12.3% clerical work, 9.1% unemployed,8.3% shopkeeper, 5.7% farmer, 3.4% higher level job and 2.8% are driver.

Table 2.2 Husbands extramarital affair reported by the participant

Variable for husband's extramarital affair	Number(n)	percentage
Before marriage:		
Participant responded yes	235	22.7
Participants responded no	738	71.4
Participants responded don't know	33	3.2
Participants do not want to reply	27	2.6
During marriage:		
Participant responded yes	166	16.1
Participants responded no	801	77.5
Participants responded don't know	38	3.7
Participants do not want to reply	28	2.7
Husbands having other wife or cohabitant:		
Participants responded yes	276	26.7
Participants responded no	695	67.3
Participants responded don't know	33	3.2
Participants do not want to reply	29	2.8
Husbands having children from other woman or wife:		
Participants responded yes	166	16.1
Participants responded no	803	77.7
Participants responded don't know	35	3.4
Participants do not want to reply	29	2.8

Table 2.2 shows that26.7% of their husband has other wife or cohabitant and among them 22.7% of their husband had extramarital affair before marriage and 16.1% had extramarital affair during marriage. Similarity in percentage of husband with extramarital affair during marriage and husband having children from other wife or cohabitant is also noted. Few percentages of women are not aware about it and few does not want to disclose this information to us.

Table 2.3 Husbands currently living with participant

Husband where about	Number (n)	Percentages
Husbands currently living with participants	619	59.9
Husband currently living somewhere else	384	37.2
Missing	30	2.9

Total	1033	100

Table 2.3 show that 37.2% of their husbands were found to live somewhere else and 59.9% are currently living together. 2.9% of missing information for this variable represents the women whose marital status is widow.

3. Reproductive Health Characteristics of Participants in the Study Population.

Table 3.1 General Reproductive Health Characteristics

Mean age at marriage (SD years) Minimum- maximum age at marriage	17.1 (3.3) 5-31
Mean age at first sex(SD years) Minimum-Maximum age at first sex	17.4(3.1) 8-32
Median age at 1st child birth, median (interquartile range years) Minimum-maximum	19 (4) 14-40
Mean for Parity of the participant, (SD number of parity) Minimum-maximum	2.6 (1.5) 0-11
Mean age at menarche(SD years) Minimum- Maximum	14.1(1.6) 11-19
Mean age at menopause(SD years) Number of participant with menopausal age (n) Minimum-maximum	46.8 (2.1) 94 31-56

Table 3.1 shows that very early age at marry with mean of 17.1 with SD of 3.3 years. Mean age at marry is almost same as mean age at first sex 17.4 with SD of 3.1years. Median age at first childbirth is 19 with inter quartile range of 4 years and mean for parity is 2.6 with SD of 1.5. Mean age at menarche and menopause are 14.1 with SD of 1.6 years and &46.8 with SD of 2.1respectively.

Table 3.2 Lifetime number of sexual partner

Lifetime number of sexual partner	Frequency (n)	Percentages
Only one	901	87.2
More than one	132	12.8
Total	1033	100

Table 3.2 shows that 87.2% of our participants had monogamous relationship.

Table 3.3 Contraceptive practice:hormonal contraceptives

Variable for hormonal contraceptives	Frequency (n)	Percentages
Current pill use	85	8.2
Pills used in past	158	15.3
Never used Pill	790	76.5
Total	1033	100
Current Depo-Provera use	94	9.1
Past Depo-Provera use	242	23.4
Never used injectables	697	67.5
Total	1033	100

In our study we have found most common mode of contraceptives that the women have used is Depo-Provera injection (32.5%), followed by Use of pills (23.5%). Among them women who are currently using pills and injectables were found to be 8.2% and 9.1% respectively.

Table 3.4 Contraceptive practice:Condom

Participants with use of condom	Frequency (n)	Percentages
Current use	42	4.1
Used only in the past	118	11.4
Never used condom	873	84.5
Total	1033	100

We have found very less use of condom among married couple. Only 4.1% reported of using condom regularly and 84.5% have never used condom.

Table 3.5 Participants with signs and symptoms of sexually transmitted disease

Participants with abnormal vaginal discharge	516(50%)
Participants with genital sore or ulcer	452(43.8%)
Participants with genital wart	207(20%)

Table 3.5 shows that highest proportion of participant 50% reported to have abnormal vaginal discharge, followed by 43.8% with genital sore or ulcer and 20% with genital wart.

Table 4. Proportion of women who had at least one Pap test within age group 16-59

Age group	Never had Pap test N (%)	At least one Pap test N (%)	Total N (%)
16-19	46 (74.1)	16 (25.8)	62 (100)
20-24	114 (73.1)	42 (26.9)	156 (100)
25-29	117 (66.4)	59 (35.5)	176 (100)
30-34	88 (57.8)	64 (42.1)	152 (100)
35-39	76 (50)	76 (50)	152 (100)
40-44	74 (52.1)	68 (47.8)	142 (100)
45-49	46 (49.4)	47 (50.5)	93 (100)
50-54	39 (69.6)	17 (30.3)	56 (100)
55-59	28 (63.6)	16 (36.3)	44 (100)
Total	628 (60.8)	405 (39.2)	1033 (100)

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	36,385[a]	8	,000
Likelihood Ratio	36,886	8	,000
Linear-by-Linear Association	12,856	1	,000
N of Valid Cases	1033		

a. 0 cells (,0%) have expected count less than 5. The minimum expected count is 17,25.

Among the 1033 participant, 405 had previous pap a least once. Among them 29% belongs to age group 16-29, 46.6% with age group 30-44 and 42% with age group 45-59.

Table 5. Pap smear result detected from this study

Pap smear result	**Participant's age into 3 categories**			**Total**	**Percentages**
	15-29	30-44	45-59		
Normal	290	343	143	776	79.4
Inflammatory	62	74	22	158	16.2
ASC-US	12	9	6	27	2.8
ASC-H	1	0	0	1	0.1
LSIL	1	1	0	2	0.2
HSIL	1	3	1	5	0.5
Unsatisfactory	1	2	5	8	0.8
Total N (%)	368	432	177	977	100

ASC: Atypical squamous cells

ASC-H: Atypical squamous cells of high-grade.

ASCUS: Atypical squamous cell of undetermined significance.

LSIL: Low grade squamous intraepithelial lesion.

HSIL: High grade squamous intraepithelial lesion.

Prevalence:

977 of 1033 participants had a Pap smear. 79.42% of Pap smear was found to be normal and 16.2% were normal but inflammatory.

Prevalence of different degree of abnormal cervical smear using TBS is as follows:

ASC: 28/977× 1000 = 2.86%= 28 per 1000 population.

(Out of 28 cases of ASC that was reported in our study 27(96.4%) of them are ASCUS and only 1(3.6%) is ASC-H)

LSIL: 2/977 × 1000 = 0.2%=2 per 1000 population.

HSIL: 5/977 × 1000 = 0.5%= 5per 1000 population.

For prevalence of different grades of abnormal cervical smear:

Total prevalence of ASC, LSIL and HSIL are taken, which is equivalent to **3.56 % = 35/1000**.

Table 5.1 Proportion of Squamous Cell Abnormalities

Participant's Age group	Proportion of Squamous Cell Abnormalities N (%)
16-29	15 (42.9)
30-44	13(37.1)
45-59	7 (20.0)
Total (16-59)	35 (100)

As shown in table 5.1, when we grouped ASC, LSIL and HSIL into abnormal squamous cell abnormalities, the proportion of abnormal cervical smear were found to be highest in age group 15-29 followed by 30-44 and least in 45-59. However overall squamous cell abnormalities is found in women aged 15-29, 60 %(3/5) of HSIL is found in women aged 30-44. This makes this age group more likely of target group for cervical cancer screening.

Table 6. Participants refusal for having Pap smear in this cervical cancer screening clinic.

Reason for not having Pap smear	Frequency	Percent
Fear of being diagnosed as cancer	17	30.4%
Ashamed of having gynaecological examination	23	41.1%
Having heavy menstruation	7	12.5%
Recently had Pap test	9	16.0%
Total	**56**	**100.%**

Total of 1033 participant, 977 had Pap smear test and 56 refused the test. Out of them 41.1%are ashamed of having gynaecological examination, 29% having fear of being diagnosed as cancer, 15.8%had recent Pap test and 12.5% are having heavy menstruation but they did not return for follow up test.

Table 7. Different Modes of Information Dissemination System used to Increase Cervical Cancer Awareness in Bharatpur, Nepal

Among 1033 total participant 608(58.9%) had claimed that they have never heard about cervical cancer.

.	Information dissemination system		
	Health worker N (%)	Relative/family/friends N (%)	Mass media N (%)
Response from the remaining 425 participants when asked about the information dissemination system from which they have acquired Knowledge about cervical cancer.	202 (47.5)	328 (77.1)	332(78.1)

Out of 425 who have heard of cervical cancer, 78.1% reported that they have heard through mass media, 77.1% through relative/ family/ friends and 47.5% through health worker. This shows that health workers role for disseminating information of cervical cancer was found less compared to mass media and social networks such as family, friends and relatives.

Table 8. Cross table of variable ever heard about cervical cancer versus ever been to School

Awareness of cervical cancer	Ever been to School		Total
	Yes N (%)	No N (%)	N (%)
Ever heard of cervical cancer	254(45.8)	169 (35.4)	423 (40.9)
Never heard of cervical cancer	301(54.2)	309 (64.6)	610 (59.1)
Total	555 (100)	478 (100)	1033 (100)

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	11,510(b)	1	,001		

A Computed only for a 2x2 table

B 0 cells (, 0%) have expected count less than 5. The minimum expected count is 195, 73.

Table 8 shows that 45.8% of women who have ever been to school have heard about cervical cancer compared to only 35.4% of women who have never been to School. This different rate of women who have heard of cervical cancer in two different groups of those who have ever been to school and never been to school is significant with P value of .001.

Table 9. Proportion of women who had Previous Pap smear among those who were aware of cervical cancer versus those women who were not aware of cervical cancer.

Previous Pap smear taken category	Cervical cancer awareness		Total N (%)
	Ever heard about cervical cancer N (%)	Never heard about cervical cancer N (%)	
Not had previous Pap smear	186 (44)	442 (72.4)	628 (60.8)
Had previous Pap smear	237 (56)	168 (27.5)	405 (39.2)
Total	423 (100)	610 (100)	1033 (100)

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	85,047[b]	1	,000		
Continuity Correction[a]	83,856	1	,000		
Likelihood Ratio	85,232	1	,000		
Fisher's Exact Test				,000	,000
Linear-by-Linear Association	84,965	1	,000		
N of Valid Cases	1033				

a. Computed only for a 2x2 table

b. 0 cells (,0%) have expected count less than 5. The minimum expected count is 165,84.

Table 9 shows that 237(56.5%) of women who have heard of cervical cancer had Pap smear compared to only 168(27.5%). This means that there is 2 times more likely chance of having Pap smear taken to those women who have heard of cervical cancer compared to those who have never heard of cervical cancer. This difference is significant with P value of 0.000.

Table 10. Proportion of women who are aware of cervical cancer among different level of schooling

Level of Schooling	**Awareness about cervical cancer**		**Total N (%)**
	Aware N (%)	Not Aware N (%)	
Illiterate	160 (34.6)	303 (65.4)	463 (44.8)
Primary	70 (38)	114 (62)	184 (17.8)
Secondary	100 (43.3)	131 (56.7)	231 (22.4)
Completed high school or higher degree	93 (60)	62 (40)	155 (15)
Total	423 (40.9)	610 (59.1)	1033 (100)

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	32,463(a)	4	,000

a 0 cells (,0%) have expected count less than 5. The minimum expected count is 31,12.

Table 10 shows that there is increase proportion of women with awareness of cervical cancer as education level increases from primary to completed high school. This difference in proportion of women in different groups of education level is significant with Chi-square value of P=0.000.

Table11. Participant's knowledge regarding cervical cancer

Variables used to assess Cervical cancer knowledge	Response from participants			
	Yes N (%)	No N (%)	I don't know N (%)	Total N (%)
Preventable	269 (26)	90(8.7)	674(65.2)	1033(100)
Treatable	255(24.7)	94(9.1)	684(66.2)	1033(100)

Table 11 shows that only 26% of the participant knows that cervical cancer is preventable if diagnosed early course of disease and 24.7% of the participant knows that cervical cancer is treatable if diagnosed early course of disease.

Table 12. Number of participant versus non participant in this study

Total study population

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	participant	1033	66,8	66,8	66,8
	non participant	514	33,2	33,2	100,0
	Total	1547	100,0	100,0	

This table shows that out of 1547 total study population 514(33.2%) are non participant.

Table13. Distribution of household of study population located at slum area versus non slum area

Distribution of household of study population

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not from slum area	786	50,8	50,8	50,8
	from slum area	761	49,2	49,2	100,0
	Total	1547	100,0	100,0	

This table shows that in our study participant from slum and non slum are almost equally represented with 50.8% household from non slum area versus 49.2% household from slum area.

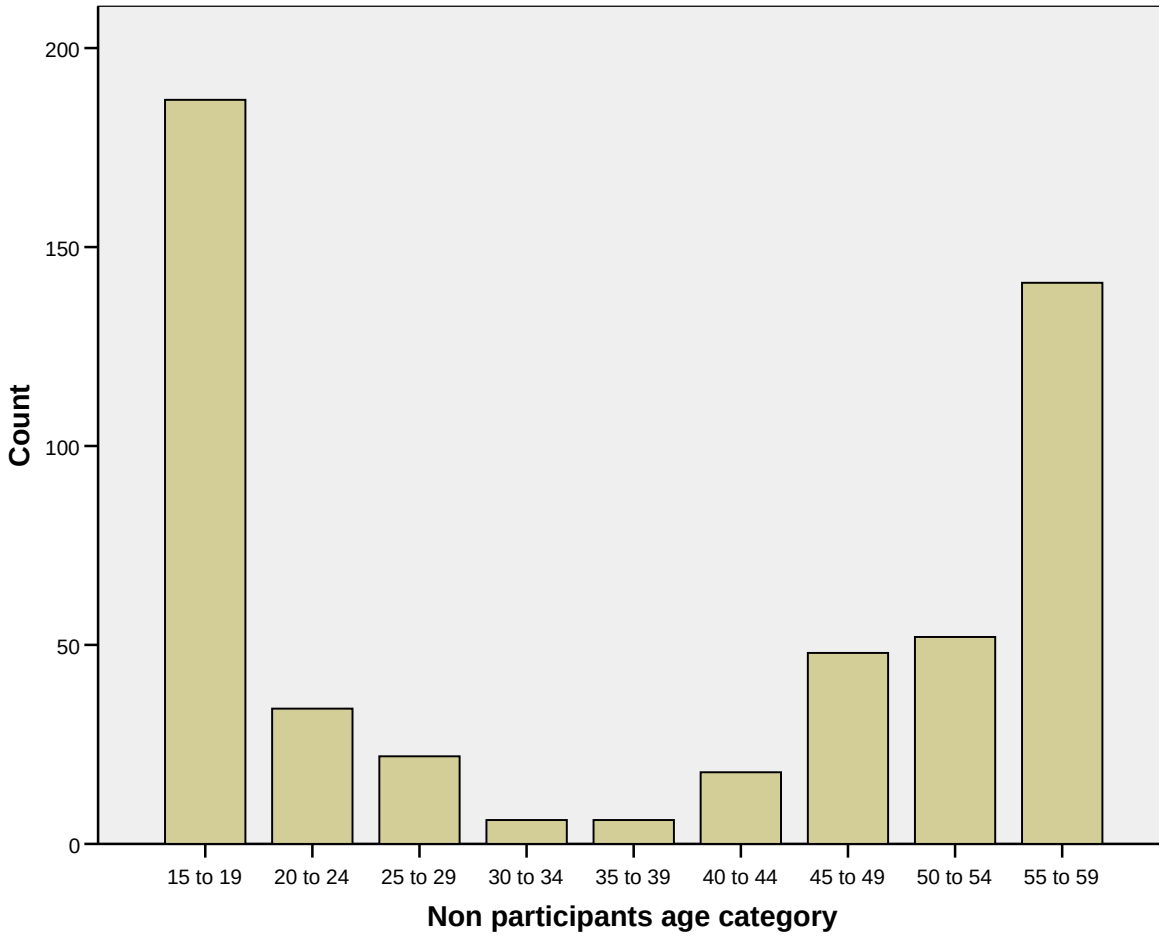
Table 14.distribution of household of non participant in slum area versus non slum area

Household distribution of non participant

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not from slum area	365	71,0	71,0	71,0
	from slum area	149	29,0	29,0	100,0
	Total	514	100,0	100,0	

This table shows that 365(71%) of non participants are from non slum area compared to 149 (29%) from slum area.

Graph 1.Distribution of non participant according to age group

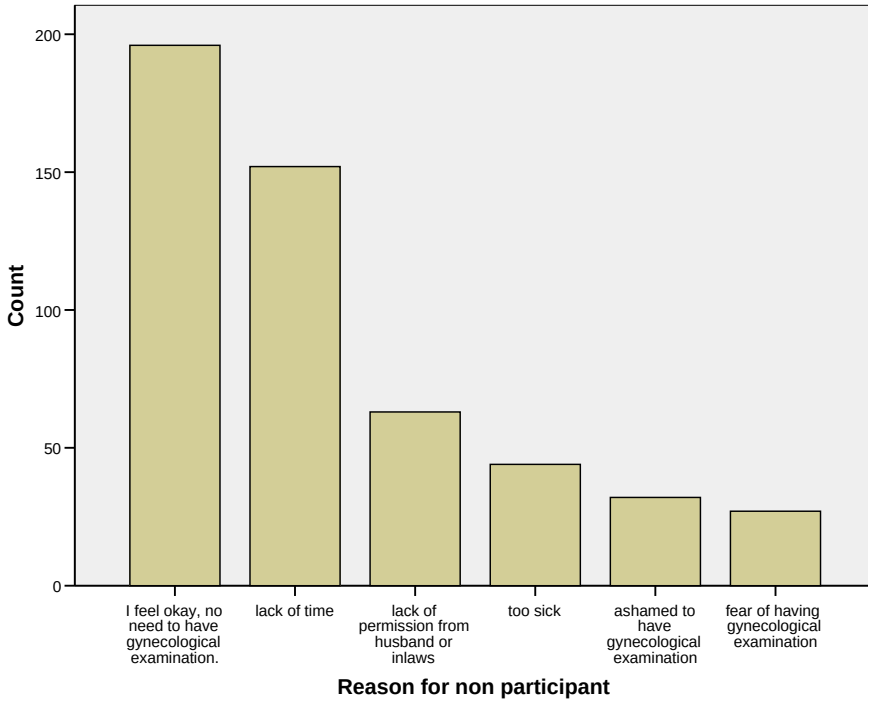


The graph shows that highest proportion of non participant are from two extreme age groups (15-19 and 54-59).This is the usual trend observed in many other studies also when it comes to participants age versus non participant rate.

Table 15. Reasons for non participant.

Reasons	Frequency
I feel okay, no need to have gynaecological examination	196(38.1%)
Lack of time	152(29.6%)
Lack of permission from husband or in-laws	63(12.3%)
Too sick to come to screening clinic	44(8.6%)
Ashamed to have gynaecological examination	32(6.2%)
Fear of having gynaecological examination	27(5.3%)
Total	514(100%)

Graph 2. Graphical representation of non participant with various reasons.



38.1% of non participant did not perceived need for Pap smear test because they feel that they are okay.29.6% of non participant lack time to come to screening clinic, 12.3% of o non

participant did not got permission from husband or in-laws to come to screening clinic, 8.6% of non participant were sick, 6.2% of non participant were ashamed to have gynaecological examination and 5.3% of women did not come to screening clinic because of fear of having gynaecological examination.

Chapter 5: Discussions

5.1 Detection Rate of Abnormal Cervical Smear and Possible Causes Behind it:

In our study we have found that the prevalence of different grades of abnormal smear (ASC, LSIL and HSIL) is 3.5% which is equivalent to 35 /1000 population. This finding of ours is some what higher than the prevalence of 2.5% abnormal smear detected on 2003, study conducted by IARC and BPKMCH in Bharatpur municipality. Probably this increment of prevalence in our study could be attributed to the sampling of the participants. In our study we have included age group 16-59 and in 2003 study age group are limited to 30-59 and Precancerous lesion, especially ASCUS and LSIL which occurs more among young sexually active women may have regressed back to normal by the age of 30 or above. The reason that we have included younger age group in this study is because in this project we also intended to find out the prevalence of HPV, which is more common in younger age groups.

Out of 28 cases of ASC that was reported in our study 27(96.4%) of them are ASCUS and only 1(3.6%) is ASC-H. This is also accordance with other study finding of Pap smear reporting done on TBS 2001.[14] Our study has found higher proportion of women with HSIL (0.5 % of total smear)compared to LSIL which is only 0.2% of total smear. This is contradictory with most other study finding that proportion of women with LSIL is usually higher than HSIL. It could be due to the fact that there is less reproducibility for LSIL than for HSIL and the rate of LSIL is more variable than rate of HSIL. [43, 44] This can be also supported by the fact that 0.5% of HSIL in our study is exactly equal to median reporting rate of HSIL, found in study conducted in USA including 2000 laboratories for inter laboratory comparison program in cervicovagnal cytology.[45] In the same study 80% laboratories reported 0.64 to 4.23 with median ASCUS/SIL ratio of 2.0. Our finding of 3.85 ASCUS/SIL ratio is accordance with upper limit of this study. Rate of unsatisfactory smear in our study is 0.8% and this is almost equal to the mean of 0.95% unsatisfactory smear found in this study.

Thus the detection rate of abnormal smear in our study is more or less similar to the reporting done in different laboratories in USA using the Bethesda system.

unsatisfactory smear noted in our study are much lower compared to other study conducted in Norway and Iceland.[33,46] 19.4% of the women who had taken cervical smear were women age more than 45 in our study and mean age for menopausal

was 46.8 with standard deviation of 2 years. Inward shift of the transformation zone toward endo-cervical canal is common among postmenopausal women and makes collection of smear difficult. [47] Therefore unsatisfactory smear of 0.8% which we found in our study could be attributed to physiological changes of the women themselves rather than inappropriate collection of specimen by smear collector.

The proportion of HSIL was found to be highest in age group 30-45 (3/5) compared to 1/5 in each age group 16-29 and 45-59. This is also accordance with another study conducted in Nepal, which showed that CIN2 and CIN 3 are common in age group31-40. [8]

According to WHO, standard approach for management of HSIL or ASC-H is to refer for colposcopy and biopsy and confirmed cases of HSIL should be treated with Cryotherpay, LEEP or Cold knife conization. In our study, this was considered from the beginning and solidarity fund was allocated for the purpose. But to our surprise, 4/5 HSIL positive in our study declined our offer to provide biopsy and treatment, despite several trial of persuasion. However no documentation was done, almost all of them said that they do not like to take out any tissue from there cervix and most of them also consulted previous women who have undergone treatment for precancerous lesion and they told them that the treatment makes them more sick with uncomfortable vaginal discharge.

Partly this is true that one of the complication of Cryotherapy is prolonged and profuse watery discharge.[13] Probably this might have cause misconception of getting more sick after the treatment. Thus we lost the follow up of these women with HSIL, which is actually one of the most important components of screening programme.

It has been already proven that persistence of high risk types of HPV is a prerequisite for development of CIN3 lesion and invasive cancer and one of the important determinants of acquisition of hrHPV is women with increase number of sexual partner.[23,24] Taking into consideration of the theory of the pathogenesis of cervical cancer which accounts infection of cervical epithelium with specific hrHPV, having cervical cancer as number one malignancy in Nepal, where most women practice monogamous relation contradicts the finding.

In a setting where the role of Sexually Transmitted infection (STI) is not explained by the characteristics of the participant then it is mandatory to identify the role of their sexual partner from whom they may have acquired. Taking into consideration of this factor we have also surveyed the characteristics of their husband and found that significant proportion 26.7% of 1033 women reported that their husband with other wife or cohabitant, 16.1% of 1033

reported husband with extramarital affair during their marriage and 22.7% of 1033 reported husband with extramarital affair before their marriage.

Significant proportion of women reported having experienced signs and symptoms of STD, such as 50% 1033 women reported that they had abnormal vaginal discharge, 43.8% with genital sore or ulcer, 20% with genital wart and 16.2% were found to have inflammatory lesion on Pap smear finding. This concludes that STI among these women are common.

Number of sexual partner of women is a sensitive issue especially in a strict society like Nepal. Therefore however we did our best to get reliable answer pertaining to lifetime number of sexual partner of women; we can not be very sure that if we have extracted the very reliable answer in this part.

Nevertheless considering that almost all of these women have monogamous relationship; their husband's extramarital affair must have played a role to acquire STI. This is further compounded by the fact that very few partners 42(4.1%) were found to use condom currently and that might have jeopardized the safer sexual behaviour and eventually lead to cervical cancer. The constraints on condom use of among men were also shown in another study conducted in Nepal. [43]

Since HPV can affect any other part of genital area where condom does not cover, regular use of condom may not have a great effect for controlling HPV as other STD such as *Chlamydia*, HSV and *Neisseria gonorrhoea.* But controlling these other STI helps acquisition of the HPV. Thus change of behaviour for safe sex is utmost important factor to control cervical cancer. Societal behavioural pattern that are risk to develop cervical cancer such as low literacy rate among women, early marriage, early childbirth, high number of parity and women who are current smoker are found to be prevalent in our study. These societal behavioural patterns of women and their husband's role of having extramarital affair and unsafe sexual behaviour may have played role to have cervical cancer as number one malignancy in Nepal.

5.2 Cervical Cancer Screening Coverage:

As it has been mentioned above that one of the element of successful screening programme is high coverage (80%) and many developing countries has failed to accomplish this by over screening younger women than the women with risk group who have high chances to develop cervical cancer (women with age 35-45).Our finding also shows similar situation in the context of Nepal.

In our study we have found that 29% of 405 women who are age group 16-29 had Pap smear at least once. From this we can conclude that present opportunistic cervical cancer screening are directed toward screening women who have less risk compared to age group over 30. Our study also showed that 46.6% of 446 women with age group 30-44 and 42% of 193 women aged group 45-59 had previous pap at least once. This relatively high coverage of cervical cancer screening among aged 30-44 and 45-59 could be due to the cervical screening provided to 5000 women aged 30-59 in 2003 while conducting Cryotherapy study between BPKMCH and IARC and the fact that women included in the study actually came to a screening, and are seriously biased toward this type of behaviour.

Many studies have shown that women with higher educational level are more likely to participate in screening clinic than with lower educational level. [(36)]Therefore another factor for relatively high coverage could be due to the fact that our study population were found to be more literate 55.2% compared to the nationwide adult female literacy rate of 28.7% according to demographic indicators of Nepal. [(4)]

Thus in reality we can predict that the coverage must be way below than what we have found in our study. Therefore our finding is over estimation if it has to represent the cervical cancer screening coverage for total population.

HSIL has highest probability of progression to invasive cancer. Based on our result with highest proportion of HSIL in age group 30-45, we can speculate that women within this age group should be the target group for cervical cancer screening in our setting. But meaningful conclusion can not be made at this point just based on 5 HSIL that we have found in our study. Thus more future researches should be carried out to find out the age specific prevalence of abnormal cervical smear to derive conclusion for specific target age group for cervical cancer screening. But to date, considering the limited resource in our country, few coverage of cervical cancer screening and yet to start organize cervical cancer screening the best and practical strategy to provide equitable cervical cancer screening service would be to include women with age group between 35-45 once in her lifetime as WHO has recommended.

Though its only one case, we have also found HSIL in age group younger than 30. Possible occurrence of HSIL in women younger than 30 years old were also shown in other previous studies.[(46,49)] This age group had also the highest proportion of ASCUS 12 (44.44%). A Meta analysis of 27,000 women showed that 0.3% of ASCUS progress to invasive cancer at 24 months.[(17)] This concludes that this age group is also not risk free. Therefore in future when more resources is available and when screening coverage for highest risk group are increase

then we should also focus our attention to include younger women with age less than 30 depending upon the age specific prevalence of abnormal cervical smear among them.

5.3 Determining Barriers to Women's Participation in Screening Clinic

Health education is needed to ensure optimal programme coverage, which in turn will lead to increase program impact. Many barriers to cancer screening programme can be addressed through education of the community.

Many studies have shown that in developing countries, barriers to cervical cancer screening uptake include absence of knowledge about the disease, lack of familiarity with the concept of preventive health care, geographic and economic inaccessibility of services, poor quality of services and lack of support from families and communities. [(36)] In our study, we have found 514(33.2%) of 1547 are non participant. In order to find out the barriers we have addressed few questionnaires to them for their reasons for non participation in this study.

We have found that majority of our non participant (38%) did not perceived need for Pap smear test because they feel that they are okay. This indicates that these women have not understood the rationale of the preventive approach of cervical cancer screening programme. This is also further supported by our finding that only 26% think that cervical cancer is preventable when diagnosed at early course of the disease. Utilization of preventive health services is not a norm in Nepal, particularly for elderly women. Therefore message about cervical cancer must include what cervical cancer is and how it can be prevented.

Significant proportion (12.3%) of women also did not have permission from their husband and probably this could be due to lack of knowledge about cervical cancer among their husband. In our part of world where society is male dominated and female literacy is still very low, woman's ability to make informed decision on about her health is not only influenced by her own beliefs and behavioural patterns, but also by her family and existing social networks. Thus for successful cervical cancer screening programme, information regarding cervical cancer should reach the husband and community at large.

Some women (5.3%) have not participated in the screening clinic due to fear of being diagnosed as cancer. Probably this is due to perception of fatalistic attitude in relation to any cancer. For this change of attitude one must be knowledgeable about the

treatable nature of cervical cancer. In our study we have found only 24.7% have correctly responded when they were asked if cervical cancer is treatable when diagnosed at early course of the disease. Thus information on cervical cancer should contain the available treatment and where it can be available.

Thus providing correct information on cervical cancer in the community and in health services is a key to raising awareness and reducing incidence and mortality. All categories of health care providers, in whatever setting they work, should provide correct and consistent information to women and men on cervical cancer, how it can be prevented, reasons for screening and the significance of it and management of any abnormality detected.

Many studies have found that characteristics of underserved women in cervical cancer screening programme are women who are older than 45 years, poorer, less educated, unemployed or working in informal sector, living in non permanent dwellings without a partner, not familiar with other women who had undergone screening and were not regular clients of health care or family planning services.[35]We were not able to assess all these variables due to lack of time but our finding in relation to household settlement from slum versus non slum shows that there were more non participant from non slum are which are economically much better than slum area. This could be due to the fact that screening services were provided free of cost so that women from slum area did their best to take this opportunity whereas women from non slum area may have not felt this opportunity as important as women from slum area since they can afford health services when they need.

Though we have not directly assessed the cost of cervical cancer screening as barrier to service utilization but from this we can derive a conclusion that if services are free of cost or at minimal price utilization of services by women from lower socio-economic condition are favourable.

In relation to age of the non participant our finding are similar to other study that most of the non participant are either too young or too old. [36]More than 90% of women belonging to age group 30-49 have participated in screening clinic. Therefore if we include our target screening age is 35-45 and frequency is once in a lifetime, based on our finding we can conclude that age will not be a problem.

5.4 Awareness and knowledge regarding cervical cancer

Several studies have found that lack of awareness about cervical cancer and how to prevent it is an important obstacle to improving cervical cancer screening coverage. [37, 38, 39, 40] Thus ACCP recommends that cervical cancer screening programme in any country must increase awareness of cervical cancer and encourage women in their 30s and 40s to be screened in order to reduce incidence and mortality from cervical cancer.

With this goal in our mind we have assessed the proportion of women who have heard of cervical cancer among our participant and found 40.9%of 1033 have heard of cervical cancer. Our study finding also shows that proportion of women who had previous Pap smear are more in women who have heard of cervical cancer than in those who have never heard. This shows that women who are aware of cervical cancer are more likely of having Pap smear.

Some discrepancy has been found between proportion of women who are aware of cervical cancer and their actual knowledge about preventive and treatable nature of cervical cancer. This is shown by the fact that however 40.9% of 1033 women have heard of cervical cancer, only 26% of women were found to know correct information when asked if cervical cancer is preventable and only 24.7% were found to know if cervical cancer is treatable.

Probably this could be attributed to the mode of information from which they have acquired this knowledge. Our finding has shown that among the 423 women who have heard of cervical cancer 47.8% have heard from health worker, 77.5% from relative, family and friends and 78.5% from mass media. Hence higher proportion of women has heard about cervical cancer through mass media and relative, family and friends compared to health worker.

Considering the low literacy rate of women in Nepal, information that they have acquired through mass media may not have understood fully or the information acquired through social networks such as family, friends and relatives may not be correct information due to lack of their own knowledge regarding the disease.

Study conducted by ACCP in Cabanas project in El Salvador [36] showed that community health workers from ministry of health (MOH), who were trained in basic issues related to cervical cancer prevention, including risk factors and the priority age range for cervical cancer screening were effective means to promote cervical cancer

screening. Similarly, in Ghana community health nurses who have integrated cervical cancer screening outreach activities into existing child welfare clinic has resulted screening coverage increase from 4.62% to 6.56% in 5 month period. [36]

FCHV programme was initiated in Nepal in 1988/89 with the objective of promoting health and at present there are 47,873 FCHV actively working all over the country. The number of FCHV to population at district is 1:400 in Terai, where our study area is located, 1:250 in hills and 1:150 in mountains. [50]

To date, the role of FCHV is mainly focussed on promotion of safe motherhood, child health, family planning and other community health services but not in promoting cervical cancer screening activities in public health approach. However it has been said that BPKMCH has trained some of the FCHV about cervical cancer screening awareness program but there role in population level were not yet found.

With the access of these already existing FCHV in community it would be cost effective to train and utilize them for disseminating information as it has been done in above Cabanas project in El Salvador. Beside this all health worker in all level and all sector should be encouraged and mobilized to disseminate proper information to eliminate the above mentioned barriers.

5.5 Strength of the study

It is a population based study so that it gives better representation of total population compared to most of the hospital based study where there is a sampling bias, since most of the women who goes to hospital are either they are sick or they are the one who have better access of health facility due to various reason.

This study is conducted in area where the precancerous lesion and cervical cancer treatment is possible. So that there will be good follow up of patient even after completion of this study. Regular follow up of women with abnormal cervical smear and proper referral of these women for needful management is crucial part of cervical cancer screening to have better impact on decrease incidence and mortality.

This study is conducted in collaboration with IARC. As the Cancer research unit of WHO, IARC generates the scientific data useful for developing cancer control policies. Hence their expert suggestion and guidance helped this study to carry out as best as possible.

Solidarity fund is allocated for follow up of abnormal cervical smear and treatment of those women who cannot afford. This had given all women in this study an equal opportunity for treatment.

To increase the validity of the Pap smear result in our study we have done our best to control the smear taker and smear reader bias.

Cervical smears were taken by very well trained doctors and nurse and cervical smear was collected using both extended tip plastic Ayre's Spatula and endocervical brush in order to assure collection of both ecto and endocervical specimen. This can be also proven by the fact that unsatisfactory smear noted in our study are much lower even than the study conducted in Norway and Iceland. [33,46] 19.4% of the women who had taken cervical smear were women age more than 45 in our study and mean age for menopausal was 46.8 with standard deviation of 2 years. Inward shift of the transformation zone toward endo-cervical canal is common among postmenopausal women.[47] Therefore unsatisfactory smear of 0.8% which we found in our study could be attributed to physiological changes of the women themselves rather than inappropriate collection of specimen by smear collector.

All our Pap smear slides were read by single pathologist. Which helped to control the inter observer bias in reporting the result. Since this pathologist had also done her doctorate thesis in Pap smear reading and her work experience in BPKMCH helped to get the Pap smear result as reliable as possible. Pap smear reading was done on TBS and this nomenclature for reporting is also recommended by WHO. Detection rate of abnormal smear in our study was found to be more or less similar to detection rate in many laboratories in U.S.A.[45] where they also used the same reporting system. This further strengthens our reliability of the result.

Data entries were done by two separate data entry personnel thus errors in recording data were controlled. Response rate for questionnaire were also found100% without missing value and though sampling process were not done by choosing women at random but at least cluster randomization was done to give the good representative sample for whole population.

Validity of questionnaires used in our study is assured by pre-testing of questionnaire during pilot study. These questionnaires were also adapted from questionnaires that were used for assessment of reproductive morbidity in Nepal [41] and in Women's Health survey in Norway. Sets of translated questionnaires from English to Nepali language were also concluded exact translation after checking by 3 Nepalese doctors. Thus by using

validated questionnaires and choosing interviewers with collage level of education secured a good quality of data collection.

Data entries were done by two separate data entry personnel thus errors in recording data were controlled. Response rate for questionnaire were also found100% without missing value and though sampling process were not done by choosing women at random but at least cluster randomization was done to give the good representative sample for whole population. Thus we tried our best to maintain the validity and representability of the study.

5.6 Weakness of the study

Quality control of the Pap smear reading should be done by either reading all negative smears or at least 10% of the negative abnormal smear should be read by another pathologist and there should be reproducibility of the same result between these two readers. But in this study we failed to do so for various reasons as mentioned above in methodology portion.

The usual recommendation for start of screening age is at the maximum prevalence of SIL lesions. But due to very few numbers in our study meaningful conclusion can not be made in this regard.

Due to the misconception of the women in the community that treatment for pre-cancer makes them more sick with more vaginal discharge made us loss of follow up for women with HSIL.Thus this limited us to provide effective treatment for these women who have high chances to have cervical cancer in future.

Ideally women who shows signs of inflammation on per speculum examination should first be treated and recall later to have Pap smear. But such practice was not followed in our study because of high possibility of loss to follow up if specimen were not collected at that time. This may give false negative Pap smear result since there is a possibility that inflammatory cells may obscure abnormal cell beneath it.

As a matter of fact 5000 women from Bharatpur municipality were offered cervical cancer screening services in 2003 and some women who were included in that study also attended this time in our study. Therefore by selecting these women we may had some response bias especially when it comes to awareness and knowledge regarding cervical cancer.

Women in our study area also represent women with better access of health service facilities, more urbanized and more literate than the other area of this district. Probably this kind of selection bias may result less representation of the total population. But considering the political unrest of our country at that time we are bound to choose a study area which is safer and practical enough to carry our daily activities.

Due to limitation of time we have assessed awareness, knowledge and determinants of women's barriers to undertake cervical cancer screening among these women by using structured questionnaire. Which may have resulted some response bias in information since most of the answers are already fixed and participants has no freedom to answer in their own way. Ideally these factor can be assessed more in depth by using open ended questionnaire or qualitative study such as focus group discussion, participatory observation etc.

Chapter 6: Conclusion

Rate of reporting of abnormal cervical smear in our study is more or less similar to the reporting done on many laboratory is USA.Though proportion of women with HSIL, which have higher chances to develop in to cervical cancer is low in our study compared to the finding in Norway and Finland, cervical cancer is number one malignancy in Nepal. Probably this can be attributed to the lack of cervical cancer screening services in Nepal.

However almost all women in our study claimed to have monogamous relationship, Societal behavioural pattern that are risk to develop cervical cancer such as low literacy rate among women, early marriage, early childbirth, high number of parity and women who are current smoker are found to be prevalent in our study. These societal behavioural patterns of women and their husband's role of having extramarital affair and unsafe sexual behaviour may have played role to have cervical cancer as number one malignancy in Nepal.

According to our study finding 29% of Pap smear coverage are among women who are younger than 30 years old and Pap smear screening coverage among 30-45 is just 45% despite completion of recent big cervical cancer screening study in the same area covering 5000 women of this age in year 2003-2004. This concludes that cervical cancer screening coverage for women with highest risk is low.

33% of the study population did not participated in the study and interestingly, these non participants are more from non slum area (area with higher socioeconomic status) compared to Slum area. This is probably due to free cervical cancer screening services that we offered in our study which made more participation rate from women with lower socioeconomic status.

Major determinants of women's barrier to utilize Pap smear clinic that we have detected in our study includes women's lack of perception for need to utilize preventive health service like screening clinic (38.1%), Women's lack of time (29.6%), lack of permission from husband to go to the screening clinic (12.3%).

In our study we found that proportions of women who have ever heard of cervical cancer are 1.4 times more likely of having previous Pap smear compared to who have never heard. This shows that awareness of cervical cancer is important factor to have increase coverage rate for cervical cancer screening.

Some discrepancy has been found between proportion of women who are aware of cervical cancer and their actual knowledge about preventive and treatable nature of

cervical cancer. Higher proportion of women in our study have heard of cervical cancer through mass media and social networks such as family, friends and relatives compared to health worker. Probably this can be attributed to either they have not understood the message completely from mass media or informant from social network may not have given correct information.

In our study we have evidenced loss to follow up of women with HSIL. This is primarily due to misconception of previous women who had treatment for precancerous lesion that it cause more sick with uncomfortable vaginal discharge. This concludes that proper counselling of these women prior giving treatment is very necessary. Otherwise they may increase the false alarm in the community and hinders success of cervical cancer screening programme.

Hence organized cervical cancer screening is necessary to increase coverage and campaign to increase awareness and knowledge regarding cervical cancer should start effectively according to the needs of community.

Chapter 7: Recommendations

Experience in developed countries as mentioned above has shown that well planned organized screening programmes with high coverage can significantly reduce incidence of cervical cancer and mortality associated with it. Therefore since the infrastructure to run cervical cancer screening already exists in Bharatpur due to BPKMCH, organized screening service in this area is highly recommendable.

Given the fact that we are at very early phase of providing cervical cancer screening services we would like to recommend more realistic approach of screening women at their 30s and 40s (who are more likely to detect precancerous lesion) at least once in their lifetime than to screen women at any age.

However this is more realistic approach, we would like to recommend future researcher to do more study to find out age specific incidence rate for precancerous lesion so that we can determine the actual target population for screening.

Despite some awareness program initiated by BPKMCH our study found that only few are aware of cervical cancer and even among these women who are aware of cervical cancer lacks actual knowledge of cervical cancer. Therefore we recommend starting more awareness program suited to the needs of community.

In a situation like our country where female literacy is low and worse in the age group 30s and 40s, probably best way to disseminate information is face to face through trained personnel about health education. Thus we recommend training existing FCHV in community in regards to cervical cancer awareness and utilizing them for disseminating information.

Based on our experience of women's misconception about the precancerous treatment and refusal to avail it despite free of cost we would like to recommend that every women who need this sort of treatment should receive thorough counselling with explaining advantage and possible disadvantage of the treatment before they receive their treatment.

Increase awareness is not only matter of disseminating information but what is most important is disseminating correct information. Therefore we would like to recommend content of the message about cervical cancer should at least be what cervical cancer is, how it can be prevented, what treatments are available if diagnosed to have precancerous lesions or invasive cancer, advantages and disadvantage of these treatment strategy and where these services are provided.

Based on our finding of women's barrier for utilization of Pap smear screening clinic we would like to recommend:

-Message that screening is a test that is applied to select asymptomatic individuals at risk of having or developing a disease should be clearly mentioned in a simple language. So that they may understand the role of preventive approach of cervical cancer screening and may realize that even women who are healthy is at risk.

- Mobile cervical cancer screening camp are highly encouraged since this may provide opportunity to those women who does not get time to go to screening clinic.

- Involvement of men and community at large for cervical cancer control is highly recommendable in order to have more women's participation in Pap smear clinic. Probably this can be done by disseminating cervical cancer information by FCHV when meeting of mothers group are held once a month. Explaining sensitive issues like sexually transmitted disease to men by FCHV may not be culturally appropriate on our part of world. Therefore men's participation in this aspect may play a better role to sensitize other men about these issue and allow there wife to have Pap smear to prevent having cervical cancer.

Husband's extramarital affair and lack of safer sexual behaviour noted in our study made us to recommend integrative approach of cervical cancer awareness with STD clinic in order to have better impact on long term cervical cancer control. STD clinic target younger age group of people than target group of cervical cancer screening women but educating these young groups of people about the consequence of unsafe sexual behaviour may prevent future occurrence of cervical cancer and also they may be crucial in persuading their family and community to utilize cervical cancer screening services in the community.

Qualitative researches to identify the barriers to participate in cervical cancer screening are also highly recommendable to find out the community's need and their perception about cervical cancer and cervical cancer screening services. Identifying these factors is essential to formulate specific information targeted to the need of community.

Evaluation of the current screening services and identifying the problems are also highly recommendable. By doing this we can find out the problem area of services and changes can be made for better.

After the international conference on population and development (ICPD) in Cairo in 1994, Nepal has also developed National Reproductive Health policy and

reproductive health of elderly including cancers was included as one of the essential components of national RH package.[51] But according to conference report which was held in Bangkok in 2005 and participated by 25 developing countries including Nepal showed that there is existence of gap in Nepal when it comes to formulate specific policy regarding cervical cancer prevention.[52]Thus this evidence based guidelines derived from our study would be helpful to implement national policies in this particular field.

ANNEXES

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Annex 2: Invitation Register

Household	**Subject identification number** (study =3 digits, subject=4 digits)	**Full name**	**Age** [1]	**Marital Status** [2]	**Date of appointment** DD/MM/YY	**Date of screening** DD/MM/YY	***Date of re-invitation*** DD/MM/YY	***Reason for non-participation*** [3]
|__|__|__|__|	|**1**||**4**||**2**|-|__||__||__||__|	|__||__|						

If the exact age is unknown, give estimation, [2]Codes for marital status: 1) single; 2) married; 3) separated or divorced; 4) widow,

[3]Codes for non-participation: 1) too sick; 2) lack of time 3) no need to have an examination or blood sample collection;

4) Fear of gynecological examination or blood sample collection; 5) lack of permission from husband/parents; 6) other.

Annex 3: Invitation card (to be completed and delivered at time of recruitment)

Invitation Card
Cervical cancer screening
BP Koirala Memorial Cancer Hospital/
World Health Organisation

Identification label

Subject identification number : |**1||4||2**|-|__||__||__||__|

Household : |__||__||__||__|

Full name : ……..……..……

Date of visit(DD/MM/YY) : |__|__|/|__||__|/|__||__|

Address of the clinic :

Annex 4 Human Papillomavirus Prevalence Surveys in Bharatpur, Nepal

INFORMED CONSENT FORM

Cervical cancer is the most common cancer in Nepalese women. It develops following the infection of the cervix by a virus, the human papillomavirus. If the lesion in the cervix is detected early, cancer can be prevented, or at least treated effectively. You are invited to participate in a study aimed at improving the prevention of cervical cancer. This study is being performed in collaboration with the International Agency for Research on Cancer, Lyon, France.

I hereby agree to participate in the Human papillomavirus (HPV) Prevalence Survey in Bharatpur, Nepal. I understand that the goal of the project is to improve the understanding and prevention of cervical cancer.

If I participate, I will be asked questions about my background, education, pregnancies, family planning, health, smoking and lifestyle. Some of the questions will be personal. I can refuse to answer any question that bothers me.

I understand that a trained midwife or physician will perform an exam of my vagina and cervix, and that, during the examination; a specimen of cells from my cervix will be taken using a specially designed plastic brush. This cervical specimen will be used to test for cervical abnormalities as well as for the presence of human papillomavirus and other infectious agents. In addition, the midwife or physician will draw a small amount of blood which will be used to test for the presence of antibodies to human papillomavirus and other infectious agents. Some of the tests on the cervical specimens and blood will be research tests. I understand that standard medical procedures will be used for all the exams and the tests used in this study.

If any disease is found as a result of the examinations, I understand that I will be notified and referred for proper additional examinations and treatment if needed.

Minor bleeding may result from the cervical examination and very rarely infection may result. There may be some minor discomfort or soreness from the blood drawing and rarely a bruise may develop. Although the risk from these procedures is minimal, in the unlikely event that there are adverse reactions, I understand that I will be treated.

All medical and personal information obtained in this study which would permit identification of any individual will be held in strict confidence and will be used only for research purposes. My name and other identifying information will not appear in any report of the study.

I understood information about the objectives of the study, benefits and risks associated with participation, and assurance of the confidentiality of the information when delivered orally to the whole group.

My participation is voluntary and I may refuse to take part in any of the study procedures at any time without penalty or loss of any benefits. For further information about this study I can contact Dr.Ang Tshering Sherpa at Himal Path Bharatpur, Tel no. 056-522292.

Please indicate whether you would like to participate in each component of the study by checking the line next to each item below:

_____ cervical cell sample collection
_____ blood sample collection
_____ risk factor questionnaire

I show my willingness to undergo the above procedures and to answer the question by putting my signature or thumb prints on this form

_____ _____
Signature Date

Study ID number:

I testify that I have, to the best of my ability read and explained the information concerning this research study to the participant whose identification number appears above.

Interviewers

_____ _____
Signature Date

Annex 5 Individual Questionnaire

IMPORTANT notes for filling the questionnaire

EVERY question should be replied to. Use the following codes :

9 (1 box) or **99** (2 boxes) for « don't know » or « do not want to reply»

8 (1 box) or **88** (2 boxes) for « does not apply »

Under NO circumstances should any box be left empty

(e.g. : to reply 2, note |_**0**_||_**2**_|)

IMPORTANT : Questionnaire should be verified immediately after completion

Identification label

1. Household |__||__||__||__| **2. Subject identification number** : |**1**||**4**||**2**|-|__||__||__||__|

3. Full name : ……

4. Age : |__||__| (**IMPORTANT** : If exact age is unknown, give an estimation **)**

5. Date of birth (DD/MM/YY) |__||__|/|__||__|/|__||__|

6. Additional contact information (telephone , address, …)

……

……

7. Date (DD/MM/YY) |__||__|/|__||__|/|__||__|

8. Name of interviewer : ……. code: |__||__|

Demographic data

9. What is your religion? (1: Hindu, 2: Buddhist, 3: Christian, 4: Muslim)

|__|

10. What is your marital status? (1: single, 2: married, 3: separated or divorced, 4: widow) |__|

11. How old were you when you first married? |__||__|

Subject identification number: |**1||4||2**|-|__||__||__||__|

12. Have you ever been to school ? (1: yes, 2: no)

|__|

13. If yes, what is your highest level of schooling? |__|

(1: primary, 2: secondary, 3: completed school leaving certificate, 4: higher degree)

14. What is your current occupation? |__|

1: unemployed

2: house-wife

3: manual work (titling field for other, cleaning, cooking, labor etc.)

4: merchant/shop-keeper (fruit and vegetables vendor, tea shop etc.)

5: clerical work (teacher, nurse, secretary, clerks)

6: professional (doctor, lawyer, engineer, project officer)

15. What is your husband's current occupation? |__|

1: unemployed

2: farmer

3: manual work (titling field for other, cleaning, cooking, labour etc.)

4: merchant/shop-keeper (fruit and vegetables vendor, tea shop etc.)

5: clerical work (teacher, nurse, secretary, clerks)

6: professional (doctor, lawyer, engineer, project officer)

7: migrant worker

8: Driver

Medical history

16. Are you currently pregnant? (1: yes, 2: no) |__|

If yes, the women should complete the questionnaire and blood sample, but should not be offered a gynaecological examination

17. Are you currently menstruating ? (1: yes, 2: no)

|__|

If yes, the women should complete the questionnaire and blood sample, and be re-invited 7-10 days from the start of her period for gynecological examination

18. Have you ever had previous screening for cervical cancer (Pap test)?

|__|

(1: yes, 2: no)

19. As far as you know, have you ever had tuberculosis? (1: yes, 2: no) |__|

20. As far as you know, have you ever had malaria? (1: yes, 2: no)

|__|

21. Have you ever had any of the following signs or symptoms? (Explain that consistency abnormal vaginal discharge can be watery, whitish, yellowish, purulent, mucoid, foul smelling and amount can vary from scanty to excessive)

Abnormal vaginal discharge (1: yes, 2: no)

|__|

Genital ulcer/genital sores (1: yes, 2: no) |__|

Genital warts (1: yes, 2: no) |__|

Subject identification number: |**1||4||2**|-|__||__||__||__|

Smoking history

22. Have you ever regularly smoked? |__|

(1: yes, currently, 2: yes, but only in the past, 3: no)

23. At what age did you start smoking? |__||__|

24. At what age did you stop smoking? |__||__|

25. How many cigarettes per day? |__||__|

26. Have you ever regularly chewed tobacco? |__|

(1: yes, currently, 2: yes, but only in the past, 3: no)

Reproductive history

27. At what age did you start menstruating?

|__||__|

28. Are you menopausal? (Over 40 and 12 months without periods)? |__|

(1: yes, 2: no)

29. If menopausal, at what age did you have your last period? |__||__|

30. Have you ever been pregnant? (1: yes, 2: no)

|__|

31. How many full-term pregnancies have you had? |__||__|

32. How old were you at your first birth? |__||__|

33. How old were you at your last birth? |__||__|

34. Have you ever had a spontaneous abortion? (1: yes, 2: no) |__|

35. If yes, how many?

|__||__|

36. Have you ever had a voluntary abortion? (1: yes, 2: no)

|__|

37. If yes, how many?

|__||__|

Subject identification number : |**1||4||2**|-|__||__||__||__|

Contraceptive history

38. Have you or your partner ever used the following contraceptives?

Pill (1: yes, currently, 2: yes, but only in the past, 3: no)

|__|

Injectable contraceptives (1: yes, currently, 2: yes, but only in the past, 3: no)

|__|

Intra-uterine device (1: yes, currently, 2: yes, but only in the past, 3: no)

|__|

Condom (1: yes, currently, 2: yes, but only in the past, 3: no)

|__|

Tubal ligation (1: yes, currently, 2: yes, but only in the past, 3: no)

|__|

Other, please specify……|_____|

For users of pill or injectable contraceptives

39. At what age did you start using this type of contraception? |__||__|

40. At what age did you stop using this type of contraception? |__||__|

(Current age for current use)

-Now I will ask you some very personal questions. If you accept to answer please be sure that this information will be kept absolutely confidential.

Sexual history

41. At what age did you first have sexual intercourse? |__||__|

42. Do you have any children who have a father other than your husband? |__|

(1: yes, 2: no)

43. In your entire life, how many men have you had sexual intercourse with? |__||__|

44. Does your husband have any other wife/cohabitant than yourself? (1: yes, 2: no) |__|

45. Does your husband have any children by a woman other than yourself? |__|

(1: yes, 2: no)

46. To your knowledge, has your partner/husband had had sexual intercourse with other women: Before becoming your partner/husband? (1: yes, 2: no) |__|

Whilst your partner/husband? (1: yes, 2: no) |__|

47. Where does your husband currently live? |__|

(1: with you, 2: elsewhere)

48. How often is your husband away from home?

|__|

(1: <1 night/month, 2: 1-3 nights/month, 3: 4-7 nights/month, 4: >7 nights/month)

Subject identification number : |**1||4||2**|-|__||__||__||__|

Clinical examination

49. Did the woman have blood sample taken? (1: yes, 2: no)

|__|

If no, please specify why not _____

50. Did the woman have sample taken for HPV? (1: yes, 2: no)

|__|

If no, please specify why not _____

51. Did the women have sample taken for Pap smear? (1: yes, 2: no)

|__|

If no, please specify why not _____

52. Pap smear test result

|__|

1: normal/ normal but inflammatory

2: ASCUS

3: ASC-H

4: AGUS/AGC

5: LSIL

6: HSIL

7: invasive cancer

53. Have you ever heard about cervical cancer prior, to our staffs visit to your house for this study purpose?

(1: yes, 2: no) |__|

If participant responded “yes” go to question number 54, 55, 56. Otherwise skip these questions and go to question number 55.

54. Did you hear from health worker?

(1: yes, 2: no) |__|

54. Did you hear from mass media?

(1: yes, 2: no) |__|

54. Did you hear from family/friends/relatives?

(1: yes, 2: no) |__|

55. In your opinion do you think women can be prevented of getting cervical cancer?

(1: yes, 2: no, 3: I don’t know) |__|

56. In your opinion do you think cervical cancer can be treated if it is diagnosed at early course of disease?

(1: yes, 2: no, 3: I don’t know) |__|

Annexs 6: Ethical Clearance from Nepal Health Research Council.

Nepal Health Research Council

NHRC

Reference: 199

Letter of Approval for Research Proposal

January 26, 2007

Dr. Ang Tshering Lama Sherpa
Principal Investigator
Title: HPV Prevalence Survey in Bharatpur, Nepal

Dear Dr. Sherpa,
This is to inform you that the above mentioned proposal submitted by you has been approved by NHRC Executive Board on January 19, 2007 (2063-10-5) after proper recommendation of Ethical Review Board (ERB). This also certifies that there is no ethical objection.

As per NHRC regulation the investigator have to strictly follow the protocol stipulated in your proposal. Any changes in objective(s), problem statement, research question or hypothesis, methodology, implementation procedure, data management and budget that may be necessary in course of the implementation of the research proposal can only be made so and implemented after prior approval from this council. Thus, it is compulsory to submit here the detail of such changes intended or desired with justification prior to instituting actual change.

Further, the researchers are directed to strictly abide by the National Ethical Guidelines published by NHRC during the implementation of your research proposal.

Lastly the researcher, as principal investigator is obliged to submit periodic progress report every 3 months and three copies of the final research report with brief presentation of the findings and the financial statement of expenditure if funded by NHRC. If an article based upon that research is likely to be published, you must take prior permission of NHRC if funded for the same.
As per your research proposal your total research amount is US$ 22,000.00 and NHRC processing fee is US$200.00.
If you have any question, please contact our research officers.
Thanking you for your kind cooperation.

Sincerely yours,

Dr. Sharad Raj Onta
Member-Secretary

Tel. (977-1) 4254220, 4227460, Fax: 977-1-4262469, 4268284, Email: nhrc@healthnet.org.np, Ramshah Path, P. O. Box 7626, Kathmandu, Nepal.
Website: http://www.nhrc.org.np